

On page 15, please <sup>✓</sup> replace the paragraph at the top of the page beginning "According to a seventh aspect of the present" with the following paragraph:

11  
According to a seventh aspect of the present invention there are provided DNA consisting essentially of a regulatory DNA capable of inducing metastasis from SEQ. ID. NO. 5:

On page 16, please <sup>✓</sup> replace the paragraph at the top of the page beginning "According to a eighth aspect of the present" with the following paragraph:

12  
According to an eighth aspect of the present invention there are provided DNA consisting essentially of a regulatory DNA capable of inducing metastasis from SEQ. ID. NO. 6:

### In The Claims

Please amend claims 1, 2, 4, 6, 7, 11, 15-17, 23 and 29 as shown below. Please cancel Claim 3. A marked up version of the amended claims is attached to this Amendment.

13  
Subject 1 (Amended) A method of screening and recovering a regulatory DNA which is not expressed as an mRNA but is capable of inducing metastasis comprising the steps of:

i. transferring fragments of human DNA of less than 1.5 kb in length from malignant, metastatic cancer cells which have been tagged at both ends with double-stranded synthetic oligonucleotides that provide restriction enzyme and unique primer sites into a cell line that produces only benign, non-metastasizing tumours when injected into a syngeneic animal;

ii. injecting the transformed cells into the syngeneic animal;

iii. selecting those animals in which metastasizing tumours have been identified; and

iv. recovering the regulatory DNA capable of inducing metastasis therefrom.

2. (Amended) The method of claim 1 wherein said fragments of human DNA are between 1.3 and 1.5 kb in length.

Please cancel claim 3.

D<sup>14</sup>  
4. (Twice Amended) The method as in claim 1, in which the cell line that produces only benign non-metastasizing tumours is a rat mammary epithelial cell line.

Sub 2 → 6. (Amended) The method of claim 5 wherein the double-stranded synthetic oligonucleotide tag has the following oligonucleotide sequence:

Primer  
5' AATCCAAGCTT GCGGCCGATCAGGCCGAATATGCGGCCGCATTAT-3'  
AGGTTCTGAACGCCGGCTAGTCCGGCTTATACGCCGGCGTAATATCGA  
HindIII SfiI NotI Defective HindIII

D<sup>15</sup>  
7. (Amended) A regulatory DNA which is not expressed as an mRNA but is capable of inducing metastasis consisting essentially of a human DNA fragment of less than 1.5 kb in length and comprising a sequence selected from the group consisting of SEQ. ID. NO. 1, SEQ. ID. NO. 2, SEQ. ID. NO. 3, SEQ. ID. NO. 4, SEQ. ID. NO. 5, and SEQ. ID. NO. 6, obtained from a malignant, metastasis cancer cell.

D<sup>16</sup>  
11. (Amended) DNA consisting essentially of a regulatory DNA which is not expressed as an mRNA but is capable of inducing metastasis and has the sequence of SEQ. ID. NO. 4.

15. (Amended) A probe specific to a regulatory DNA which is not expressed as an mRNA but is capable of inducing metastasis as claimed in claim 7.

D<sup>17</sup>  
Sub 3 → 16. (Amended) A kit for diagnosing the likelihood of a cancer metastasizing comprising a probe of claim 15 and one or more of a color indicator, an oligonucleotide primer, materials for gel analysis and materials for DNA transfer or hybridisation.

D<sup>17</sup>  
17. (Amended) A medicament adapted to target a regulatory DNA which is not expressed as an mRNA but is capable of inducing metastasis as claimed in claim 7.

D<sup>18</sup>  
23. (Amended) A probe specific to a regulatory DNA which is not expressed as an mRNA but is capable of inducing metastasis as claimed in claim 11.

D<sup>19</sup>  
29. (Amended) A medicament adapted to target a regulatory DNA which is not expressed as an mRNA but is capable of inducing metastasis as claimed in claim 11.

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**In The Abstract**

Please insert the following Abstract(which is also provided on a separate page):

The invention relates to metastasis inducing DNA's, a method of identifying such DNA's and their use in diagnosis and therapy. It includes a method of screening and recovering met-DNA comprising the steps of: (i) transferring fragments of human DNA from malignant, metastatic cancer cells into a cell line that produces only benign, non-metastasizing tumors when injected into a syngeneic animal; (ii) injecting the transformed cells into the syngeneic animal; (iii) selecting those animals in which metastasizing tumors have been identified; and (iv) recovering the met-DNA therefrom.

**REMARKS**

Claims 1-2, 4-7, 11, 15-19, 23 and 29 are pending in this application. Claim 3 has been cancelled.

The specification has been amended to place it in the preferred layout as required by 37 C.F.R. § 1.821(a)(1) and (a)(2). An Abstract of the disclosure has also been inserted as required by 37 C.F.R. § 1.72(b). The Abstract is identical to that of the International PCT application. As such, no new matter has been added.

Claims 6, 11 and 23 were objected to under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.